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(51) International Patent Classification ⁶ : C12N 15/12, 15/16, A61K 48/00, 38/39, C07K 14/47, A61L 27/00		A3	(11) International Publication Number: WO 95/22611
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(22) International Filing Date: 21 February 1995 (21.02.95)			
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(71) Applicant: THE REGENTS OF THE UNIVERSITY OF MICHIGAN [US/US]; Wolverine Tower, Room 2071, 3003 South State Street, Ann Arbor, MI 48109-1280 (US).			Published <i>With international search report. Before the expiration of the time limit for amending the claims and to be republished in the event of the receipt of amendments.</i>
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(54) Title: METHODS AND COMPOSITIONS FOR STIMULATING BONE CELLS**(57) Abstract**

Disclosed are methods, compositions, kits and devices for use in transferring nucleic acids into bone cells *in situ* and/or for stimulating bone progenitor cells. Type II collagen and, particularly, osteotropic genes, are shown to stimulate bone progenitor cells and to promote bone growth, repair and regeneration *in vivo*. Gene transfer protocols are disclosed for use in transferring various nucleic acid materials into bone, as may be used in treating various bone-related diseases and defects including fractures, osteoporosis, osteogenesis, imperfecta and in connection with bone implants.

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INTERNATIONAL SEARCH REPORT

Intern'l Application No
PCT/US 95/02251

A. CLASSIFICATION OF SUBJECT MATTER
 IPC 6 C12N15/12 C12N15/16 A61K48/00 C07K14/47 A61K38/39
 A61L27/00

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
 IPC 6 A61K C12N A61L C07K

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	WO,A,92 05199 (GENETICS INSTITUTE) 2 April 1992 see page 12 - page 15 ---	17,26, 65, 77-128
A	DE,A,42 19 626 (WEHLING) 23 December 1993 see the whole document ---	1
A	TRENDS IN GENETICS, vol.8, no.3, pages 97 - 102 V. ROSEN ET AL. 'The BMP proteins in bone formation and repair' see the whole document ---	1
A	WO,A,93 05751 (CREATIVE BIOMOLECULES) 1 April 1993 see the whole document ---	1
		-/-

Further documents are listed in the continuation of box C.

Patent family members are listed in annex.

* Special categories of cited documents :

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- 'P' document published prior to the international filing date but later than the priority date claimed

- 'T' later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
- 'X' document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
- 'Y' document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art
- 'A' document member of the same patent family

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Date of the actual completion of the international search

27 July 1995

Date of mailing of the international search report

29.12.95

Name and mailing address of the ISA

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Internat'l Application No

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C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	WO,A,94 01139 (Baylor College of Medicine) 20 January 1994	1-16, 18-25, 59-64, 66-76 17,26, 65, 77-128
Y	see the whole document -----	

INTERNATIONAL SEARCH REPORT**Box I Observations where certain claims were found unsearchable (Continuation of item 1 of first sheet)**

This international search report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. Claims Nos.: 2, 3, 27, 28, 149

because they relate to subject matter not required to be searched by this Authority, namely:

Remark: Although these claims are directed to a method of treatment of (diagnostic method practised on) the human/animal body, the search been carried out and based on the alleged effects of the compound/composition.

2. Claims Nos.:

because they relate to parts of the international application that do not comply with the prescribed requirements to such an extent that no meaningful international search can be carried out, specifically:

3. Claims Nos.:

because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box II Observations where unity of invention is lacking (Continuation of item 2 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

1. claims 1-128
2. claims 129-131
3. claims 132-155

See continuation sheet PCT/ISA/210

1. As all required additional search fees were timely paid by the applicant, this international search report covers all searchable claims.
2. As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.
3. As only some of the required additional search fees were timely paid by the applicant, this international search report covers only those claims for which fees were paid, specifically claims Nos.:
4. No required additional search fees were timely paid by the applicant. Consequently, this international search report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

1-128

Remark on Protest

- The additional search fees were accompanied by the applicant's protest
- No protest accompanied the payment of additional search fees.

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INTERNATIONAL SEARCH REPORT

International Application No. PCT/US95/02251

FURTHER INFORMATION CONTINUED FROM PCT/ISA/210

1. Compositions devices and methods for therapy of bone diseases comprising nucleic acid
 2. Latent TGF-beta binding protein-3 (LTBP-3) and DNA encoding it
 3. Compositions devices and methods for therapy of bone diseases comprising Type II collagen.
-

INTERNATIONAL SEARCH REPORT

Information on patent family members

Inter. Appl. No.
PCT/US 95/02251

Patent document cited in search report	Publication date	Patent family member(s)		Publication date	
WO-A-9205199	02-04-92	EP-A-	0550625	14-07-93	
DE-A-4219626	23-12-93	NONE			
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